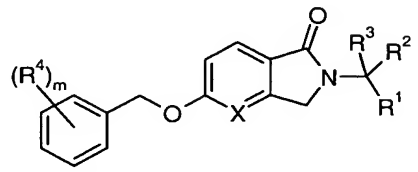
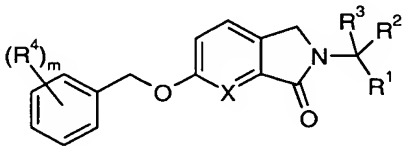
Claims

1. A compound of formula I or II



(I)



(II)

wherein

X is –N= or –CH=;

R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_p-OR^8$;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is (C_1-C_6)-alkyl, halogen, halogen-(C_1-C_6)-alkyl, C_1-C_6-alkoxy or halogen-(C_1-C_6)-alkoxy;

R^5 and R^6 are each independently hydrogen or C_1-C_6-alkyl;

R^7 is C_1-C_6-alkyl;

R^8 is hydrogen or C_1-C_6-alkyl;

m is 1, 2 or 3;

n is 0, 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

2. A compound of claim 1 wherein m is 1 or 2.

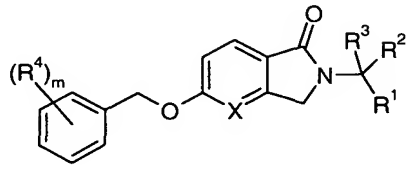
3. A compound of claim 2 wherein m is 1.

4. A compound of claim 1 wherein R^4 is halogen or halogen-(C_1-C_6)-alkyl.

5. A compound of claim 4 wherein R^4 is fluorine or trifluoromethyl.

6. A compound of claim 1 wherein X is -CH=.

7. A compound of formula I



(I)

wherein

X is –N= or –CH=;

R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_p-OR^8$;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is (C_1-C_6)-alkyl, halogen, halogen-(C_1-C_6)-alkyl, C_1-C_6-alkoxy or halogen-(C_1-C_6)-alkoxy;

R^5 and R^6 are each independently hydrogen or C_1-C_6-alkyl;

R^7 is C_1-C_6-alkyl;

R^8 is hydrogen or C_1-C_6-alkyl;

m is 1, 2 or 3;

n is 0, 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

8. A compound of claim 7 wherein R^3 is hydrogen.

9. A compound of claim 7 wherein m is 1 or 2.

10. A compound of claim 9 wherein m is 1.

11. A compound of claim 7 wherein R^2 is hydrogen or C_1-C_6-alkyl.

12. A compound of claim 11 wherein R^2 is hydrogen.

13. A compound of claim 11 wherein R^2 is methyl.

14. A compound of claim 7 wherein R^1 is $CONH_2$ or CH_2OCH_3.

15. A compound of claim 7 wherein R^8 is C_1-C_6-alkyl.

16. A compound of claim 15 wherein R^1 is $-(CH_2)_p-OR^8$.

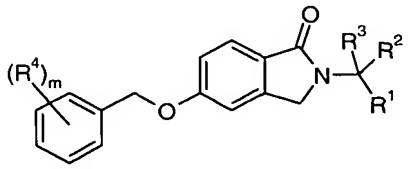
17. A compound of claim 15 wherein R^1 is $-(CH_2)_n-CO-NR^5R^6$ or $-(CH_2)_p-OR^8$; R^5 and R^6 are hydrogen; n is 0; and p =1.

18. A compound of claim 7 wherein R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_p-OR^8$; R^5 and R^6 are hydrogen; n is 0 or 1; and p is 1.

19. A compound of claim 7 wherein X is -N=.

20. A compound of claim 7 wherein X is $-CH_2-$.

21. A compound of formula I



(Ia)

wherein

R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_p-OR^8$;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is (C_1-C_6)-alkyl, halogen, halogen-(C_1-C_6)-alkyl, C_1-C_6-alkoxy or halogen-(C_1-C_6)-alkoxy;

R^5 and R^6 are each independently hydrogen or C_1-C_6-alkyl;

R^7 is C_1-C_6-alkyl;

R^8 is hydrogen or C_1-C_6-alkyl;

m is 1, 2 or 3;

n is 0, 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

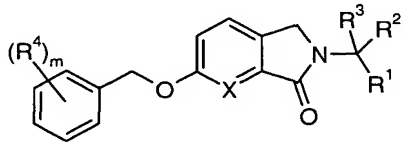
22. A compound of claim 21 wherein R^1 is -$(CH_2)_n$-CO-NR^5R^6.

23. A compound of claim 21 wherein R^1 is -$(CH_2)_n$-CO-NR^5R^6, -$(CH_2)_n$-$COOR^7$, -$(CH_2)_n$-CN, -$(CH_2)_n$-isoindole-1,3-dionyl, or -$(CH_2)_p$-OR^8; R^3 is hydrogen; R^4 is halogen or halogen-(C_1-C_6)-alkyl; R^5 and R^6 are hydrogen; m is 1 or 2; n is 0 or 1; and p is 1.

24. A compound of claim 21 wherein R^1 is -$(CH_2)_n$-CO-NR^5R^6 or -$(CH_2)_p$-OR^8; R^2 is hydrogen or C_1-C_6-alkyl; R^3 is hydrogen; R^4 is halogen or halogen-(C_1-C_6)-alkyl; R^5 and R^6 are hydrogen; R^8 is C_1-C_6-alkyl; m is 1; n is 0; and p is 1.

25. A compound of claim 21 wherein R^1 is CO-NH_2 or CH_2OCH_3; R^2 is hydrogen or methyl; R^3 is hydrogen; R^4 is fluorine or trifluoromethyl; and m is 1.

26. A compound of formula II



(II)

wherein

X is –N= or –CH=;

R^1 is -$(CH_2)_n$-CO-NR^5R^6, -$(CH_2)_n$-NR^5R^6, -$(CH_2)_n$-$COOR^7$, -$(CH_2)_n$-CN, -$(CH_2)_n$-isoindole-1,3-dionyl, or -$(CH_2)_p$-OR^8;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is (C_1-C_6)-alkyl, halogen, halogen-(C_1-C_6)-alkyl, C_1-C_6-alkoxy or halogen-(C_1-C_6)-alkoxy;

R^5 and R^6 are each independently hydrogen or C_1-C_6-alkyl;

R^7 is C_1-C_6-alkyl;

R^8 is hydrogen or C_1-C_6-alkyl;

m is 1, 2 or 3;

n is 0, 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

27. A compound of claim 26 wherein m is 1.

28. A compound of claim 26 wherein R^3 is hydrogen.

29. A compound of claim 26 wherein R^1 is -$(CH_2)_n$-CO-NR^5R^6.

30. A compound of claim 26 wherein R^1 is -$(CH_2)_n$-$COOR^7$.

31. A compound of claim 26 wherein R^1 is -$(CH_2)_n$-NR^5R^6.

32. A compound of calim 26 wherein R^2 is hydrogen or C_1-C_6-alkyl.

33. A compound of claim 32 wherein R^2 is hydrogen.

34. A compound of claim 32 wherein R^2 is methyl.

35. A compound of claim 26 wherein R^4 is halogen or halogen-(C_1-C_6)-alkyl.

36. A compound of claim 35 wherein R^4 is fluorine or trifluoromethyl.

37. A compound of claim 26 wherein R^8 is C_1-C_6-alkyl.

38. A compound of claim 37 wherein R^1 is -$(CH_2)_p$-OR^8.

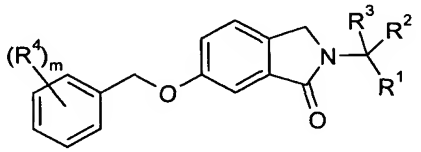
39. A compound of claim 37 wherein R^1 is -$(CH_2)_n$-CO-NR^5R^6, -$(CH_2)_n$-NR^5R^6, -$(CH_2)_n$-$COOR^7$, -$(CH_2)_n$-CN, or -$(CH_2)_p$-OR^8; R^5 and R^6 are hydrogen; n is 0; and p is 1.

40. A compound of claim 37 wherein R^1 is -$(CH_2)_n$-CO-NR^5R^6, -$(CH_2)_n$-NR^5R^6, -$(CH_2)_n$-$COOR^7$, or -$(CH_2)_p$-OR^8 and m is 1.

41. A compound of claim 26 wherein R^1 is $CONH_2$, CH_2NH_2, $COOCH_3$, or CH_2OCH_3.

42. A compound of claim 26 wherein X = -N=.

43. A compound of formula IIa



(IIa)

R^1 is -$(CH_2)_n$-CO-NR^5R^6, -$(CH_2)_n$-NR^5R^6, -$(CH_2)_n$-$COOR^7$, -$(CH_2)_n$-CN, -$(CH_2)_n$-isoindole-1,3-dionyl, or -$(CH_2)_p$-OR^8;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is (C_1-C_6)-alkyl, halogen, halogen-(C_1-C_6)-alkyl, C_1-C_6-alkoxy or halogen-(C_1-C_6)-alkoxy;

R^5 and R^6 are each independently hydrogen or C_1-C_6-alkyl;

R^7 is C_1-C_6-alkyl;

R^8 is hydrogen or C_1-C_6-alkyl;

m is 1, 2 or 3;

n is 0, 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

44. A compound of claim 43 wherein R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, or $-(CH_2)_p-OR^8$; R^2 is hydrogen or C_1-C_6-alkyl; R^3 is hydrogen; R^4 is halogen or halogen-(C_1-C_6)-alkyl; R^5 and R^6 are hydrogen; R^8 is C_1-C_6-alkyl; m is 1; n is 0; and p is 1.

45. A compound of claim 43 wherein R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, or $-(CH_2)_p-OR^8$; R^2 is hydrogen or C_1-C_6-alkyl; R^3 is hydrogen; R^4 is halogen or halogen-(C_1-C_6)-alkyl; R^5 and R^6 are hydrogen; R^8 is C_1-C_6-alkyl; m is 1; n is 0; and p is 1.

46. A compound of claim 43 wherein R^1 is $CONH_2$, CH_2NH_2, $COOCH_3$, CH_2OCH_3; R^2 is hydrogen or methyl; R^3 is hydrogen; R^4 is fluorine or trifluoromethyl; and m is 1.

47. A compound selected from
2-[5-(3-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-acetamide,
2-[5-(3-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-propionamide,
(S)-2-[6-(3-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-propionamide,
(R)-2-[6-(3-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-propionamide,
2-[5-(4-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-acetamide, or
2-[1-oxo-5-(4-trifluoromethyl-benzyloxy)-1,3-dihydro-isoindol-2-yl]-acetamide.

48. A compound which is 5-(3-fluoro-benzyloxy)-2-(2-methoxy-ethyl)-2,3-dihydro-isoindol-1-one.

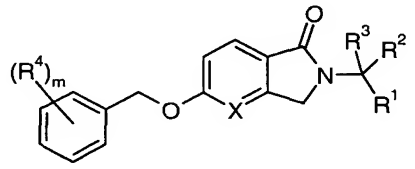
49. A compound selected from
2-[6-(3-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-acetamide,
(R)-2-[6-(3-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-propionamide,
(S)-2-[1-oxo-6-(4-trifluoromethyl-benzyloxy)-1,3-dihydro-isoindol-2-yl]-propionamide,
and
(R)-2-[1-oxo-6-(4-trifluoromethyl-benzyloxy)-1,3-dihydro-isoindol-2-yl]-propionamide.

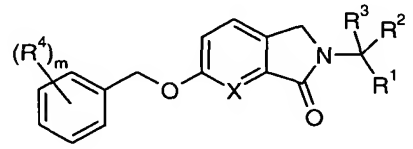
50. A compound selected from
[6-(3-fluoro-benzyloxy)-1-oxo-1,3-dihydro-isoindol-2-yl]-acetic acid methyl ester and
[1-oxo-6-(4-trifluoromethyl-benzyloxy)-1,3-dihydro-isoindol-2-yl]-acetic acid methyl ester.

51. A compound selected from
2-(2-methoxy-ethyl)-6-(3-fluoro-benzyloxy)- 2,3-dihydro-isoindol-1-one and
2-(2-methoxy-ethyl)-6-(4-trifluoromethyl-benzyloxy)-2,3-dihydro-isoindol-1-one.

52. A compound selected from
2-(2-amino-ethyl)-6-(4-trifluoromethyl-benzyloxy)-2,3-dihydro-isoindol-1-one 1:1 hydrochloride and
2-(2-amino-ethyl)-6-(4-trifluoromethyl-benzyloxy)-2,3-dihydro-isoindol-1-one 1:1 hydrochloride.

53. A composition comprising a compound of formula I or II


(I)


(II)

wherein

X is –N= or –CH=;

R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_P-OR^8$;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is (C_1-C_6)-alkyl, halogen, halogen-(C_1-C_6)-alkyl, C_1-C_6-alkoxy or halogen-(C_1-C_6)-alkoxy;

R^5 and R^6 are each independently hydrogen or C_1-C_6-alkyl;

R^7 is C_1-C_6-alkyl;

R^8 is hydrogen or C_1-C_6-alkyl;

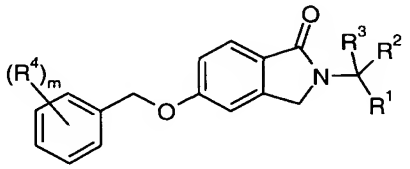
m is 1, 2 or 3;

n is 0, 1 or 2; and

p is 1 or 2;

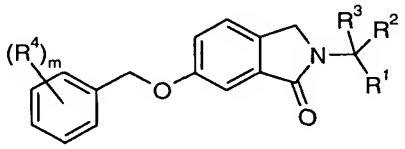
or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

54. A composition of claim 53 wherein the compound is a compound of formula Ia



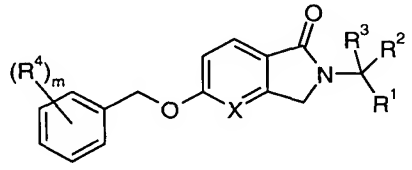
(Ia) .

55. A composition of claim 53 wherein the compound is a compound of formula IIa

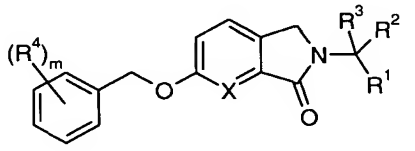


(IIa).

56. A method of treating Alzheimer's disease by administering to an individual an effective amount of a compound of formula I or II



(I)



(II)

wherein

X is –N= or –CH=;

R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_p-OR^8$;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is (C_1-C_6)-alkyl, halogen, halogen-(C_1-C_6)-alkyl, C_1-C_6-alkoxy or halogen-(C_1-C_6)-alkoxy;

R^5 and R^6 are each independently hydrogen or C_1-C_6-alkyl;

R^7 is C_1-C_6-alkyl;

R^8 is hydrogen or C_1-C_6-alkyl;

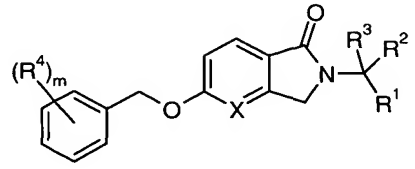
m is 1, 2 or 3;

n is 0, 1 or 2; and

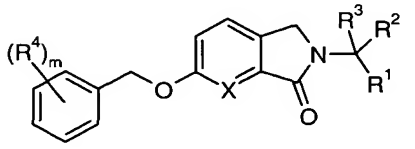
p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

57. A method of treating Parkinson's disease by administering to an individual an effective amount of a compound of formula I or II



(I)



(II)

wherein

X is –N= or –CH=;

R^1 is $-(CH_2)_n-CO-NR^5R^6$, $-(CH_2)_n-NR^5R^6$, $-(CH_2)_n-COOR^7$, $-(CH_2)_n-CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_p-OR^8$;

R^2 is hydrogen, C_1-C_6-alkyl, or OH;

R^3 is hydrogen or C_1-C_6-alkyl;

R^4 is $(C_1\text{-}C_6)$-alkyl, halogen, halogen-$(C_1\text{-}C_6)$-alkyl, $C_1\text{-}C_6$-alkoxy or halogen-$(C_1\text{-}C_6)$-alkoxy;

R^5 and R^6 are each independently hydrogen or $C_1\text{-}C_6$-alkyl;

R^7 is $C_1\text{-}C_6$-alkyl;

R^8 is hydrogen or $C_1\text{-}C_6$-alkyl;

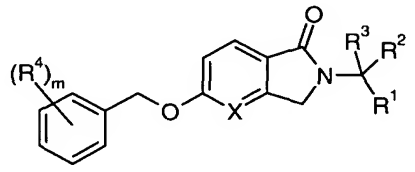
m is 1, 2 or 3;

n is 0, 1 or 2; and

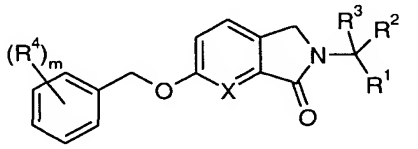
p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

58. A method of treating senile dementia by administering to an individual an effective amount of a compound of formula I or II



(I)



(II)

wherein

X is –N= or –CH=;

R^1 is $-(CH_2)_n\text{-}CO\text{-}NR^5R^6$, $-(CH_2)_n\text{-}NR^5R^6$, $-(CH_2)_n\text{-}COOR^7$, $-(CH_2)_n\text{-}CN$, $-(CH_2)_n$-isoindole-1,3-dionyl, or $-(CH_2)_p\text{-}OR^8$;

R^2 is hydrogen, $C_1\text{-}C_6$-alkyl, or OH;

R^3 is hydrogen or $C_1\text{-}C_6$-alkyl;

R^4 is $(C_1\text{-}C_6)$-alkyl, halogen, halogen-$(C_1\text{-}C_6)$-alkyl, $C_1\text{-}C_6$-alkoxy or halogen-$(C_1\text{-}C_6)$-alkoxy;

R^5 and R^6 are each independently hydrogen or $C_1\text{-}C_6$-alkyl;

R^7 is $C_1\text{-}C_6$-alkyl;

R^8 is hydrogen or $C_1\text{-}C_6$-alkyl;

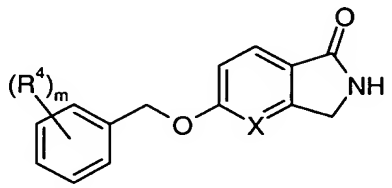
m is 1, 2 or 3;

n is 0, 1 or 2; and

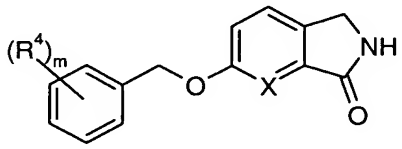
p is 1 or 2;

or a pharmaceutically acceptable salt thereof.

59. A process for the preparation of a compound of claim 1 comprising reacting a compound of formula III or V



(III)



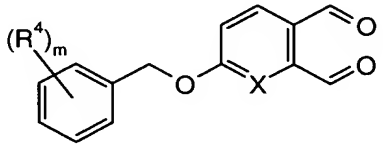
(V)

with a compound of formula IV

$$BrCR^1R^2R^3 \quad (IV).$$

60. A process for the preparation of a compound of claim 1 and pharmaceutically acceptable salts thereof, comprising

dissolving a compound of formula VIa



(VIa)

which is then treated with a compound of formula VII

$$H_2NCR^1R^2R^3 \quad (VII).$$